Test Type: CHRONIC

**Route: SKIN APPLICATION** Species/Strain: RATS/F 344

### P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane

**CAS Number:** 111-91-1

F1\_R2

C Number: C99028

Lock Date: 07/12/2005

**Cage Range:** ALL

**Date Range:** ALL

**Reasons For Removal:** ALL

**Removal Date Range:** ALL

**Treatment Groups:** Include ALL

**TDMSE Version:** 1.9.1 Date Report Regsted: 11/12/2007

Time Report Regsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Reqsted: 11/12/2007

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG
Disposition Summary				
•				
Animals Initially in Study Early Deaths	50	50	50	50
Moribund Sacrifice	21	17	31	20
Natural Death	8	4	5	6
Survivors Moribund Sacrifice		1		
Terminal Sacrifice	21	28	14	24
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Inflammation Ulcer		1 [4.0] 1 [4.0]		
Intestine Large, Cecum	(49)	(50)	(50)	(50)
Edema	1 [3.0]	()	()	()
Inflammation	1 [3.0]	4 [4 0]		
Parasite Metazoan Intestine Large, Colon	(50)	1 [1.0] (50)	(50)	(50)
Parasite Metazoan		2 [1.5]		(00)
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan Intestine Small, Duodenum	11 [1.5] (50)	5 [1.4] (50)	7 [2.0] (50)	7 [1.4] (50)
Inflammation	(30)	(50)	(50)	1 [3.0]
Ulcer		1 [2.0]		1 [3.0]
Epithelium, Hyperplasia Intestine Small, Ileum	(50)	1 [2.0] (50)	(50)	(50)
Inflammation	(50)	1 [2.0]	(30)	(30)
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Liver	(50)	(50)	(50)	(50)
Angiectasis Basophilic Focus	1 [2.0] 19	7 [1.0] 19	3 [1.0] 16	6 [1.2] 19
Clear Cell Focus	22	24	14	22
Degeneration, Cystic	6 [1.5]	5 [1.4]	10 [1.4]	15 [1.5]
Eosinophilic Focus Fatty Change	10 19 [1.5]	15 20 [1.6]	8 16 [1.6]	11 20 [1.3]
i ally Orialige	19 [1.0]	20 [1.0]	10 [1.0]	20 [1.0]

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

**Route: SKIN APPLICATION** 

Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Regsted: 11/12/2007

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Fibrosis	39 [1.2]	25 [1.3]	23 [1.2]	31 [1.2]	
Hematopoietic Cell Proliferation	2 [2.0]		• •		
Hepatodiaphragmatic Nodule	4	5	6	9	
Inflammation	32 [1.0]	38 [1.0]	33 [1.0]	41 [1.0]	
Mixed Cell Focus	4	10	8	3	
Necrosis	4 [2.5]	2 [1.5]	5 [1.8]	3 [2.0]	
Thrombosis			2 [2.5]		
Bile Duct, Cyst		1 [1.0]		1 [1.0]	
Bile Duct, Hyperplasia	46 [1.9]	46 [1.9]	44 [1.8]	47 [1.8]	
Centrilobular, Necrosis	1 [1.0]	4 [2.0]	8 [1.8]	4 [2.5]	
Mesentery	(10)	(10)	(9)	(9)	
Accessory Spleen	1 [1.0]	,	( )	,	
Fat, Necrosis	8 [2.9]	9 [2.2]	8 [2.9]	8 [2.4]	
Oral Mucosa	(2)	(0)	(0)	(0)	
Inflammation, Granulomatous	1 [3.0]	(-)	(-)	(-)	
Gingival, Cyst	2 [3.0]				
Pancreas	(50)	(50)	(50)	(50)	
Acinus, Atrophy	17 [1.8]	21 [1.6]	17 [1.6]	17 [1.5]	
Acinus, Hyperplasia	2 [2.0]	1 [2.0]	1 [1.0]	3 [1.7]	
Duct, Cyst	11 [1.6]	5 [1.8]	4 [1.8]	5 [1.4]	
Salivary Glands	(50)	(50)	(50)	(50)	
Stomach, Forestomach	(50)	(50)	(50)	(50)	
Inflammation	()	2 [3.5]	6 [3.3]	10 [2.6]	
Ulcer		2 [3.5]	2 [4.0]	7 [3.0]	
Epithelium, Hyperplasia	2 [1.5]	1 [3.0]	1 [2.0]	1 [2.0]	
Stomach, Glandular	(50)	(50)	(50)	(50)	
Ectopic Tissue	1	()	()	()	
Inflammation	1 [3.0]	2 [2.0]	1 [3.0]		
Mineralization	[]	1 [1.0]	[]		
Ulcer	1 [3.0]	1 [3.0]	1 [3.0]		
ARDIOVASCULAR SYSTEM					
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	46 [1.7]	48 [1.4]	45 [1.2]	49 [1.8]	
Fibrosis	50 [1.9]	50 [2.3]	49 [2.6]	49 [2.5]	
Inflammation, Chronic Active	1 [2.0]				
Thrombosis	3 [2.3]	1 [2.0]	4 [3.0]	3 [3.3]	
Coronary Artery, Inflammation		1 [2.0]			

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

**Route: SKIN APPLICATION** 

Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Date Report Reqsted: 11/12/2007

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Lab: BAT

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Endothelium, Hyperplasia Myocardium, Infiltration Cellular, Mononuclear Cell	1 [2.0] 50 [1.9]	50 [2.3]	49 [2.6]	50 [2.5]	
Myocardium, Necrosis Myocardium, Vacuolization Cytoplasmic	50 [1.0] 50 [1.9]	50 [1.0] 50 [2.3]	49 [1.0] 49 [2.6]	50 [1.0] 50 [2.5]	
ENDOCRINE SYSTEM					
Adrenal Cortex Atrophy	(50) 1 [3.0]	(50)	(50)	(50)	
Hyperplasia Vacuolization Cytoplasmic	16 [1.5] 33 [1.3]	22 [1.4] 38 [1.3]	13 [1.2] 35 [1.3]	16 [1.7] 39 [1.6]	
Adrenal Medulla Angiectasis	(50)	(50) 1 [2.0]	(50)	(50) 2 [3.0]	
Hemorrhage Hyperplasia	1 [3.0]		8 [1.9]		
Islets, Pancreatic	9 [1.8] (50)	7 [1.3] (50)	(50)	10 [2.1] (50)	
Hyperplasia Parathyroid Gland	4 [1.3] (49)	9 [1.6] (44)	11 [1.4] (45)	5 [1.6] (47)	
Hyperplasia Hyperplasia, Focal		1 [3.0]		1 [2.0]	
Pituitary Gland Angiectasis Atrophy	(49) 37 [2.9] 1 [3.0]	(50) 30 [2.8]	(50) 26 [2.7]	(50) 32 [2.6]	
Cyst	6 [1.2]	6 [1.3]	10 [2.0]	8 [1.5]	
Pars Distalis, Hyperplasia Thyroid Gland	13 [2.1] (50)	16 [2.1] (50)	12 [2.1] (50)	17 [2.2] (50)	
Cyst Inflammation	1 [1.0]	1 [1.0] 1 [2.0]	1 [2.0]	1 [2.0]	
C-cell, Hyperplasia Follicle, Cyst	21 [1.5]	22 [1.3] 1	23 [1.5]	14 [1.5]	
Follicle, Hyperplasia	1 [2.0]	4 [1.8]	1 [2.0]	2 [1.5]	

### **GENERAL BODY SYSTEM**

None

#### **GENITAL SYSTEM**

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

**Route: SKIN APPLICATION** 

Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37

Date Report Regsted: 11/12/2007

First Dose M/F: 09/16/02 / 09/17/02

Suppurative 1 [2.0] (50) (50) (50) (50) (50) (50) (50) (50)
1 [2.0] (0) (0) (1) (0) (1) (0) (0) (1) (0) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (1) (0) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1
(0) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (1) (0) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1
(0) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (0) (1) (1) (0) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1
(50) (50) (50) (50) (50) (50) (50) (50)
3 [2.0] 2 [3.0] 1 [2.0] 2 [2.5] 1 [2.0] 1 [2.0] 2 [2.5] 1 [2.0] 1 [2.0] 2 [2.5] 1 [4.0
3 [2.0] 2 [3.0] 1 [2.0] 2 [2.5] 1 [2.0] 1 [2.0] 2 [2.5] 1 [2.0] 1 [2.0] 2 [2.5] 1 [4.0
1 [2.0]   2 [2.5]   47 [1.9]   49 [1.8]   1 [4.0]   (50)
50 [1.8]   50 [1.8]   47 [1.9]   49 [1.8]   1 [4.0]   (50)   (5
(50) (50) (50) (50) (50) (50)  39 [1.2] 41 [1.1] 39 [1.2] 40 [1.2]  44 [1.8] 37 [1.7] 32 [1.8] 42 [1.8]  Suppurative 1 [2.0] (50) (50) (50) (50)  2 [2.0] (50) (50) (50) (50)  Granulomatous 1 [1.0] 1 [2.0]  nelium, Atrophy 2 [4.0] 1 [4.0] 1 [2.0]  nelium, Mineralization 1 [1.0] 1 [2.0]  S SYSTEM  (50) (50) (50) (50) (50)  2 [2.0]  1 [1.0] (50) (50) (50)  2 [2.0]  1 [2.0]  2 [2.0]  5 (50) (50) (50) (50)  4 [3.3]  3 [3.3] 1 [2.0] 4 [3.3]  3 [3.3] (4) (0) (6) (5)  1 [2.0]
(50) (50) (50) (50) (50) (50) (50) (50)
39 [1.2]
Suppurative   44 [1.8]   37 [1.7]   32 [1.8]   42 [1.8]
Suppurative 1 [2.0] (50) (50) (50) (50) (50) (50) (50) (50)
(50) (50) (50) (50) (50) (50) (50) (50)
2 [2.0] (50) (50) (50) (50) (50) (50) (50) (50)
Granulomatous (50) (50) (50) (50) (50)  1 [1.0]  1 [2.0]  1 [2.0]  1 [2.0]  1 [2.0]  1 [2.0]  2 [2.0]  2 [2.0]  C SYSTEM  (50) (50) (50) (50)  4 [3.3]  3 [3.3] 1 [2.0] 4 [3.3] 2 [3.5]  (4) (0) (6) (5)  Ectasia
Granulomatous  1 [1.0]  1 [2.0]  1 [2.0]  1 [2.0]  1 [2.0]  1 [2.0]  1 [2.0]  2 [2.0]  2 [2.0]  5 (50)  (50)  (50)  (50)  (4 [3.3]  (4)  (0)  (6)  (5)  (5)  (5)  (5)  (6)  (7)  (7)  (8)  (9)  (9)  (9)  (9)  (10
1 [2.0] nelium, Atrophy 2 [4.0] 1 [4.0] 1 [2.0] nelium, Mineralization 1 [1.0] 2 [2.0] SYSTEM  (50) (50) (50) (50) (50) 4 [3.3] 3 [3.3] 1 [2.0] 4 [3.3] 2 [3.5] (4) (0) (6) (5) , Ectasia
nelium, Atrophy 2 [4.0] 1 [4.0] 1 [2.0] 2 [2.0] 1 [1.0] 2 [2.0] 2 [2.0] 3 [1.0] 3 [1.0] 3 [1.0] 4 [3.3] 3 [3.3] 4 [3.3] 4 [3.3] 2 [3.5] (4) (0) (6) (5) (5) (5) (5) (5) (5) (5) (5) (5) (5
1 [1.0] 1 [2.0] 2 [2.0]  C SYSTEM  (50) (50) (50) (50) (50) (50) (50) (50)
1 [1.0]  C SYSTEM  (50) (50) (50) (50) (50) (50) (50) (50)
(50) (50) (50) (50) (50) (50) (50) (50)
4 [3.3] 3 [3.3] 1 [2.0] 4 [3.3] 2 [3.5] (4) (0) (6) (5) , Ectasia 1 [2.0]
3 [3.3] 1 [2.0] 4 [3.3] 2 [3.5] (4) (0) (6) (5) , Ectasia 1 [2.0]
(4) (0) (6) (5) , Ectasia 1 [2.0]
, Ectasia 1 [2.0]
and the second s
, Hyperplasia, Lymphoid 1 [2.0] 1 [2.0]
yperplasia, Lymphoid 1 [2.0]
esenteric (50) (50) (50)
1 [3.0]
ymphoid 1 [1.0]
Chronic Active 1 [1.0]
(50) (50) (49) (50)
3 [1.7] 4 [2.3]
2 [1.5] 1 [3.0]

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

TDMS No. 99028 - 05
Test Type: CHRONIC

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

First Dose M/F: 09/16/02 / 09/17/02 Lab: BAT

Date Report Regsted: 11/12/2007

Time Report Reqsted: 14:57:37

Species/Strain: RATS/F 344

**Route: SKIN APPLICATION** 

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Hematopoietic Cell Proliferation	24 [1.4]	25 [1.4]	15 [1.9] 1 [2.0]	24 [1.5]	
Stromal Hyperplasia Thymus	(49)	(50)	1 [4.0] (50)	(48)	
Atrophy	45 [3.5]	50 [3.7]	46 [3.7]	47 [3.8]	
Ectopic Parathyroid Gland	1 [1.0]				
Ectopic Thyroid				1 [1.0]	
INTEGUMENTARY SYSTEM					
Mammary Gland	(49)	(50)	(50)	(50)	
Hyperplasia	13 [1.2]	10 [1.2]	7 [1.1]	12 [1.3]	
Skin	(50)	(50)	(50)	(50)	
Cyst Epithelial Inclusion	1 [2.0]	3 [3.0]			
Edema	1 [2.0]				
Hemorrhage		1 [3.0]			
Artery, Site Of Application - Dermis, Inflammation		1 [2.0]			
Control Dermis, Fibrosis			1 [2.0]		
Dermis, Inflammation		1 [2.0]	1 [2.0]		
Hair Follicle, Site Of Application -	1 [4.0]	. [=.0]			
Epidermis, Atrophy	. []				
Sebaceous Gland, Hyperplasia			1 [2.0]		
Site Of Application - Dermis, Fibrosis		1 [1.0]			
Site Of Application - Dermis,	2 [1.0]	2 [1.0]	2 [1.0]		
Inflammation					
Site Of Application - Epidermis,		1 [2.0]	1 [1.0]		
Hyperkeratosis Site Of Application - Epidermis, Ulcer	1 [1 0]				
Site Of Application - Epidermis, Olcer	1 [1.0]				
MUSCULOSKELETAL SYSTEM					
Bone	(50)	(50)	(50)	(50)	
Osteopetrosis	, ,	` '	1 [2.0]	,	
Joint, Inflammation	2 [1.0]			1 [1.0]	
Skeletal Muscle	(1)	(0)	(1)	(0)	

### **NERVOUS SYSTEM**

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Reqsted: 11/12/2007

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Brain	(50)	(50)	(50)	(50)	
Hemorrhage	1 [3.0]	,	,	,	
Hydrocephalus	17 [2.9]	14 [2.9]	14 [3.0]	14 [3.0]	
Hippocampus, Necrosis		,	1 [2.0]	11	
Hypothalamus, Compression	17 [3.4]	8 [3.4]	12 [3.5]	14 [3.3]	
Thalamus, Necrosis	[]	- []	1 [2.0]	[0.0]	
Spinal Cord	(1)	(1)	(0)	(0)	
RESPIRATORY SYSTEM					
Lung	(50)	(50)	(50)	(50)	
Congestion		1 [2.0]			
Inflammation	17 [1.2]	22 [1.2]	20 [1.3]	16 [1.0]	
Metaplasia, Osseous	1 [1.0]				
Alveolar Epithelium, Hyperplasia	7 [2.0]	12 [1.5]	9 [1.9]	8 [1.6]	
Artery, Hyperplasia		1 [2.0]			
Nose	(50)	(49)	(50)	(49)	
Foreign Body	7	12	4	5	
Inflammation	27 [1.5]	32 [1.8]	22 [1.6]	18 [1.7]	
Polyp, Inflammatory	1 [1.0]				
Glands, Cyst		1 [2.0]	2 [2.0]	1 [1.0]	
Olfactory Épithelium, Accumulation, Hyaline Droplet	1 [2.0]	2 [3.0]			
	5 [1 2]	17 [1 3]	30 [1 3]	48 [1 9]	
Olfactory Epithelium, Metaplasia					
	J [2.1]	3 [2.0]	0 [1.0]	4 [2.0]	
	1 [1 0]				
	1 [1.0]				
	(50)	(50)	(50)	(50)	
		(50)		(30)	
SPECIAL SENSES SYSTEM					
Eye	(50)	(50)	(50)	(50)	
Cataract		1 [3.0]	` '		
	2 [3.0]	1 [3.0]		2 [3.5]	
Sclera, Metaplasia, Osseous	38 [1.6]		28 [1.5]		
Harderian Gland					
	(/	(/			
Glands, Cyst Olfactory Epithelium, Accumulation, Hyaline Droplet Olfactory Epithelium, Degeneration Olfactory Epithelium, Metaplasia, Respiratory Olfactory Epithelium, Metaplasia, Squamous Trachea Inflammation  SPECIAL SENSES SYSTEM Eye		1 [2.0] 2 [3.0] 17 [1.3] 9 [2.0] (50) (50) 1 [3.0] 1 [3.0] 35 [1.6] (50)	2 [2.0]  30 [1.3] 3 [1.3]  (50) 3 [1.7]  (50)  28 [1.5] (50) 1 [1.0]	1 [1.0]  48 [1.9] 4 [2.0]  (50)  (50)  2 [3.5] 2 [3.5] 32 [1.5] (50) 2 [1.0]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Reqsted: 11/12/2007

Lab: BAT

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

FISCHER 344 RATS MALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Hyperplasia	0.14.01	1 [1.0]	0.14.51	1 [1.0]	
Inflammation	3 [1.3]	3 [1.0]	2 [1.5]	1 [1.0]	
Pigmentation, Porphyrin Zymbal's Gland	1 [2.0] (1)	(0)	(0)	(1)	
JRINARY SYSTEM					
Kidney Fibrosis	(50)	(50)	(50)	(50) 1 [3.0]	
Infarct		1 [2.0]		1 [0.0]	
Inflammation		. []		1 [3.0]	
Nephropathy Renal Tubule, Cyst	47 [1.8]	48 [1.9] 1 [2.0]	43 [1.7]	48 [2.1]	
Renal Tubule, Hyperplasia		. [=.0]		1 [1.0]	
Renal Tubule, Pigmentation, Lipofuscin	1 [3.0]			,	
Urinary Bladder Inflammation	(50)	(50)	(50)	(50) 2 [3.5]	
Muscularis, Mineralization		1 [1.0]			
Transitional Epithelium, Hyperplasia	1 [2.0]		1 [2.0]	1 [2.0]	

<sup>\*\*\*</sup> END OF MALE \*\*\*

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

**Route: SKIN APPLICATION** Species/Strain: RATS/F 344

### P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane **CAS Number:** 111-91-1

First Dose M/F: 09/16/02 / 09/17/02

Date Report Regsted: 11/12/2007

Time Report Reqsted: 14:57:37

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG
Disposition Summary				
Animals Initially in Study Early Deaths	50	50	50	50
Moribund Sacrifice	19	18	15	19
Natural Death Survivors	12	2	7	13
Terminal Sacrifice	19	30	28	18
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Intestine Large, Cecum	(50)	(50)	(50)	(50)
Intestine Large, Colon	(50)	(50)	(50)	(50)
Parasite Metazoan	3 [1.0]	3 [1.0]	2 [2.5]	1 [1.0]
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan		4 [3.0]	6 [1.7]	5 [1.8]
Ulcer	1 [2.0]			
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Ulcer	1 [4.0]			
Liver	(50)	(50)	(50)	(50)
Angiectasis	4 [1.0]	5 [1.2]	1 [1.0]	2 [1.0]
Basophilic Focus	41	48	42	30
Clear Cell Focus	9	9	10	5
Degeneration, Cystic	_	2 [1.0]	-	-
Eosinophilic Focus	5	8	6	6
Fatty Change	9 [1.7]	9 [1.4]	4 [1.5]	9 [1.6]
Fibrosis	5 [1.0]	3 [1.0]	10 [1.0]	2 [1.5]
Hepatodiaphragmatic Nodule	7	6	8	8
Inflammation	40 [1.0]	45 [1.0]	39 [1.1]	33 [1.0]
Mixed Cell Focus Necrosis	4	10	10	3
	2 [1.0]	1 [1.0]	2 [1.5] 1 [1 0]	1 [1.0]
Bile Duct, Cyst Bile Duct, Hyperplasia	17 [1.3]	1 [2.0] 18 [1.3]	1 [1.0] 19 [1.6]	12 [1.6]
Centrilobular, Necrosis	4 [2.5]	3 [3.0]	5 [2.0]	5 [1.8]
Periportal, Cytoplasmic Alteration	4 [2.5] 1 [2.0]	၁ [၁.0]	ال.ك] د	J [1.0]
Mesentery	(13)	(13)	(17)	(6)

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Reqsted: 11/12/2007

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Necrosis	1 [3.0]				
Fat, Necrosis	13 [2.5]	12 [2.6]	17 [2.5]	6 [3.0]	
Oral Mucosa	(1)	(0)	(0)	(0)	
Pancreas	(50)	(50)	(50)	(50)	
Hyperplasia	(30)	1 [2.0]	(30)	(30)	
Inflammation	2 [2.5]	1 [2.0]		1 [1.0]	
Acinus, Atrophy	2 [2.5] 13 [1.4]	12 [1.2]	9 [1.3]	6 [1.3]	
Acinus, Aurophy Acinus, Hyperplasia	1 [2.0]	12 [1.2]	9 [1.5]	0 [1.3]	
Duct, Cyst	4 [1.8]	6 [1.5]	1 [2.0]	2 [1.0]	
Stomach, Forestomach	4 [1.8] (50)	(50)	(50)	2 [1.0] (50)	
Inflammation	6 [3.2]		(50) 1 [2.0]	(50) 2 [3.0]	
	0 [3.2]	3 [3.0]	1 [2.0]		
Ulcer	4 [3.3]	3 [3.0]		1 [2.0]	
Epithelium, Hyperplasia	1 [4.0]	2 [2.0]	(50)	(50)	
Stomach, Glandular	(50)	(50)	(50)	(50)	
Fibrosis	0.00.01			1 [2.0]	
Inflammation	2 [2.0]			1 [3.0]	
Mineralization	4.54.01	4.54.03		2 [1.5]	
Ulcer	1 [1.0]	1 [1.0]	(0)	2 [2.5]	
Tongue	(0)	(0)	(0)	(1)	
ARDIOVASCULAR SYSTEM					
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	40 [1.2]	45 [1.1]	42 [1.1]	46 [1.6]	
Fibrosis	50 [1.5]	50 [2.0]	50 [2.0]	50 [2.3]	
Thrombosis	1 [3.0]	1 [3.0]		55 [2.5]	
Coronary Artery, Inflammation	1 [2.0]	[]			
Myocardium, Infiltration Cellular,	50 [1.5]	50 [2.0]	50 [2.0]	50 [2.3]	
Mononuclear Cell	00[1.0]	00 [2.0]	00 [2.0]	00 [2.0]	
Myocardium, Necrosis	50 [1.0]	50 [1.0]	50 [1.0]	50 [1.0]	
Myocardium, Vacuolization Cytoplasmic	50 [1.5]	50 [2.0]	50 [2.0]	50 [2.3]	
Myodardidin, Vacadiizatidii Gytopiadiiilo	00 [1.0]	00 [2.0]		00 [2.0]	
NDOCRINE SYSTEM					
Adrenal Cortex	(50)	(50)	(50)	(50)	
Angiectasis	1 [3.0]	, ,	, ,	1 [2.0]	
Hemorrhage				2 [2.5]	
Hyperplasia	11 [1.7]	26 [1.5]	18 [1.7]	14 [1.6]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

TDMS No. 99028 - 05
Test Type: CHRONIC

**Route: SKIN APPLICATION** 

Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Regsted: 11/12/2007

Lab: BAT

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG
Vacuolization Cytoplasmic	15 [1.7]	17 [1.5]	21 [1.7]	15 [1.3]
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	1 [2.0]	3 [1.3]	3 [1.7]	4 [1.8]
Necrosis			1 [3.0]	
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	10 [1.0]	6 [1.0]	5 [1.0]	6 [1.0]
Parathyroid Gland	(43)	(46)	(48)	(50)
Pituitary Gland	(50)	(50)	(50)	(50)
Angiectasis	32 [2.6]	39 [2.5]	32 [2.3]	26 [2.4]
Atrophy	1 [2.0]			
Cyst	16 [1.4]	21 [1.6]	17 [1.5]	18 [1.4]
Hemorrhage				1 [1.0]
Pars Distalis, Hyperplasia	16 [2.1]	26 [1.8]	19 [2.1]	18 [2.3]
Pars Intermedia, Hyperplasia	1 [2.0]			
Thyroid Gland	(50)	(50)	(50)	(50)
Atrophy	,	,	1 [3.0]	,
Cyst			1 [1.0]	
C-cell, Hyperplasia	33 [1.5]	38 [1.4]	34 [1.3]	19 [1.2]
Follicle, Hyperplasia		2 [2.0]	3 [1.7]	

### **GENERAL BODY SYSTEM**

None

### GENITAL SYSTEM

Clitoral Gland	(50)	(50)	(50)	(50)
Cyst	1 [2.0]	2 [2.5]	2 [2.0]	
Hyperplasia	2 [3.0]	6 [2.0]	6 [1.8]	3 [1.0]
Inflammation	32 [1.4]	32 [1.3]	40 [1.4]	23 [1.4]
Ovary	(50)	(50)	(50)	(50)
Atrophy	, ,	2 [4.0]	2 [4.0]	, ,
Cyst	5 [2.4]	4 [1.8]	7 [1.7]	5 [2.0]
Bilateral, Cyst			1 [2.0]	
Uterus	(50)	(50)	(50)	(50)
Atrophy	1 [2.0]	, ,	, ,	, ,
Inflammation, Suppurative	1 [1.0]			
Cervix, Endometrium, Hyperplasia		1 [3.0]		
Cervix, Myometrium, Hyperplasia	1 [3.0]			

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Reqsted: 11/12/2007

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Endometrium, Hyperplasia, Cystic Vagina	6 [1.7] (0)	4 [1.8] (0)	4 [1.0] (0)	5 [2.0] (1)	
HEMATOPOIETIC SYSTEM					
Bone Marrow	(50)	(50)	(50)	(49)	
Atrophy	2 [2.0]	,	` ,	,	
Hyperplasia	3 [2.7]	1 [2.0]	2 [3.0]	3 [2.7]	
Lymph Node	(3)	(1)	(5)	(1)	
Deep Cervical, Hyperplasia, Lymphoid	(3)	( · )	1 [2.0]	(.,	
Mediastinal, Ectasia		1 [3.0]	1 [2.0]		
Mediastinal, Hyperplasia, Lymphoid	1 [1.0]	1 [5.0]			
Pancreatic, Ectasia	1 [3.0]				
Pancreatic, Hyperplasia, Lymphoid	1 [3.0]				
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)	
		(50)	(50)	(50)	
Hyperplasia, Lymphoid	1 [1.0]	(50)	(50)	(50)	
Spleen	(50)	(50)	(50)	(50)	
Atrophy	3 [1.7]			2 [2.5]	
Fibrosis				1 [1.0]	
Hematopoietic Cell Proliferation	29 [1.7]	37 [1.4]	34 [1.6]	26 [1.8]	
Infarct				1 [3.0]	
Thymus	(49)	(50)	(50)	(49)	
Atrophy	43 [3.2]	50 [3.5]	47 [3.4]	35 [3.3]	
Hemorrhage				1 [3.0]	
INTEGUMENTARY SYSTEM					
Mammary Gland	(50)	(50)	(50)	(50)	
Hyperplasia	5 [1.4]	(00)	3 [2.0]	2 [3.5]	
Inflammation	1 [1.0]		O [2.0]	2 [0.0]	
Skin	(50)	(50)	(50)	(49)	
Cyst Epithelial Inclusion	(30)	(30)	(30)	(43)	
Control Dermis, Inflammation	1 [2.0]				
	1 [2.0] 1 [2.0]				
Control Epidermis, Hyperplasia	1 [Z.U]	1 [2 0]	1 [2 0]		
Dermis, Inflammation		1 [2.0]	1 [2.0]		
Epidermis, Hyperplasia		1 [2.0]	4 [0 0]		
Epidermis, Ulcer		1 [2.0]	1 [2.0]		
Sebaceous Gland, Hyperplasia			1 [1.0]		
Site Of Application - Dermis, Fibrosis	3 [1.0]		1 [2.0]	1 [1.0]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

Time Report Reqsted: 14:57:37 First Dose M/F: 09/16/02 / 09/17/02

Date Report Regsted: 11/12/2007

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Site Of Application - Dermis,		2 [1.5]	3 [2.0]	2 [1.5]	
Inflammation Site Of Application - Epidermis,			1 [1.0]		
Hyperkeratosis Site Of Application - Epidermis, Hyperplasia	1 [2.0]	2 [2.5]	5 [1.8]	1 [2.0]	
Site Of Application - Epidermis, Ulcer Subcutaneous Tissue, Necrosis	1 [2.0]	1 [2.0]	3 [2.0] 1 [3.0]	1 [2.0]	
MUSCULOSKELETAL SYSTEM					
Bone Joint, Inflammation	(50) 1 [1.0]	(50)	(50)	(50) 3 [1.3]	
NERVOUS SYSTEM					
Brain	(50)	(50)	(50)	(50)	
Hemorrhage Hydrocephalus	1 [3.0] 11 [3.2]	14 [3.0]	8 [3.5]	5 [2.4]	
Hippocampus, Necrosis Hypothalamus, Compression Vein, Infiltration Cellular, Mononuclear Cell	13 [3.3]	1 [2.0] 12 [3.6] 1 [2.0]	8 [4.0]	5 [2.6]	
RESPIRATORY SYSTEM					
Lung Congestion Inflammation Metaplasia, Osseous	(50) 1 [2.0] 18 [1.1]	(50) 31 [1.0]	(50) 2 [2.0] 24 [1.1] 1 [1.0]	(50) 1 [3.0] 19 [1.1]	
Thrombosis Alveolar Epithelium, Hyperplasia Alveolar Epithelium, Metaplasia, Squamous	1 [2.0] 1 [2.0]	7 [1.6]	7 [1.4] 3 [1.3]	6 [1.5]	
Bronchus, Hyperplasia Nose Foreign Body	(49) 1	1 [2.0] (49) 2	(50) 2	(49)	
Inflammation	10 [1.5]	14 [1.1]	16 [1.3]	6 [1.3]	

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

# P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

bis(2-Chloroethoxy)methane CAS Number: 111-91-1

First Dose M/F: 09/16/02 / 09/17/02 Lab: BAT

Date Report Regsted: 11/12/2007

Time Report Reqsted: 14:57:37

Route: SKIN APPLICATION
Species/Strain: RATS/F 344

FISCHER 344 RATS FEMALE	0 MG/KG	75 MG/KG	150 MG/KG	300 MG/KG	
Glands, Cyst				1 [2.0]	
Olfactory Epithelium, Accumulation, Hyaline Droplet		1 [2.0]	1 [2.0]		
Olfactory Epithelium, Degeneration	5 [1.0]	4 [1.3]	18 [1.1]	49 [2.3]	
Olfactory Epithelium, Metaplasia,			1 [1.0]	1 [1.0]	
Respiratory				4 [4 0]	
Olfactory Epithelium, Metaplasia, Squamous				1 [1.0]	
Respiratory Epithelium, Degeneration			1 [1.0]		
Trachea	(50)	(50)	(50)	(50)	
Glands, Cyst		1 [2.0]			
PECIAL SENSES SYSTEM					
Eye	(50)	(50)	(50)	(50)	
Cataract	1 [3.0]	2 [3.0]	3 [3.0]	5 [2.8]	
Retina, Atrophy	2 [2.0]	3 [2.7]	4 [2.8]	5 [3.0]	
Sclera, Metaplasia, Osseous	7 [1.6]	2 [2.0]	6 [1.3]	4 [1.3]	
Harderian Gland Hyperplasia	(50)	(50)	(50) 1 [1.0]	(50)	
Inflammation	5 [1.0]	11 [1.0]	9 [1.0]	10 [1.2]	
Capillary, Hyperplasia	0[0]	1 [1.0]	0 [0]	. • [=]	
Lacrimal Gland	(0)	(1)	(0)	(0)	
Hyperplasia	(2)	1 [2.0]	(5)	(4)	
Zymbal's Gland	(0)	(0)	(0)	(1)	
RINARY SYSTEM					
Kidney	(50)	(50)	(50)	(50)	
Hydronephrosis	1 [3.0]	1 [3.0]	1 [3.0]	1 [2.0]	
Inflammation, Suppurative Nephropathy	30 [1.3]	1 [3.0] 30 [1.2]	34 [1.1]	25 [1.2]	
Renal Tubule, Cyst	30 [1.3] 1 [2.0]	30 [1.2]	3 <del>4</del> [1.1]	20 [1.2]	
Urinary Bladder	(50)	(50)	(49)	(50)	
Inflammation	1 [3.0]	. ,		, ,	
Transitional Epithelium, Hyperplasia			1 [2.0]		

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

**Route: SKIN APPLICATION** Species/Strain: RATS/F 344

### P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH **AVERAGE SEVERITY GRADES[b]**

bis(2-Chloroethoxy)methane **CAS Number:** 111-91-1

First Dose M/F: 09/16/02 / 09/17/02

Date Report Regsted: 11/12/2007

Time Report Reqsted: 14:57:37

Lab: BAT

**FISCHER 344 RATS FEMALE** 

0 MG/KG

**75 MG/KG** 

150 MG/KG

300 MG/KG

\*\*\* END OF REPORT \*\*\*

a - Number of animals examined microscopically at site and number of animals with lesion

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)